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SUMM . This invention comprises at least one of the fat-soluble vitamins provitamin D, previtamin D, **vitamin D**, active **vitamin D**, vitamin K or an analog of one of these mixed in a cosmetic or **sunscreen**, and applied topically to the skin in order to prevent exposure of the skin to harmful UV in the neighborhood. . . . the form of the solution, ointments, creams, lotions, sprays and treatment conditioners which have conventionally been used in cosmetics and **sunscreens**. Since the use of cosmetics on the skin inhibits the skin's synthesis of **vitamin D** by UV light, it is also possible to supplement **vitamin D** through the skin using the dermatological composition containing **vitamin D** adapted to a cosmetic.

SUMM . . . pili activity, and prevents hair loss. In other words, the use of conventional dermatological compositions interferes with the synthesis of **vitamin D** in the skin. One way of supplying **vitamin D** to the skin is through the topical use of the dermatological composition containing the vitamins D ergocalciferol and **cholecalciferol** of this invention on the skin and hair. The concentration of provitamin D, previtamin D, **vitamin D**, active **vitamin D** or vitamin K in the ophthalmic or dermatological composition for protecting against harmful UV radiation of this invention, since it. . . topical administration, may be about 100 micrograms/ml(g) or less, or at least about 0.01 micrograms/ml(g). Since provitamin D, previtamin D, **vitamin D**, active **vitamin D** and vitamin K are not cytotoxic, they should not affect the ocular tissue or epidermal cells if used in a normal mixture. When the ophthalmic composition or dermatological composition of this invention is used, the provitamin D, previtamin D, **vitamin D**, active **vitamin D** or vitamin K which covers the eyes or skin absorbs a significant amount of harmful UV radiation, and protects ocular and skin tissue from harmful UV radiation. If conventional **vitamin D** and active **vitamin D** preparations are taken orally in large doses, symptoms of **vitamin D** excess occur. Calcium and phosphates rise in the blood, and there is calcification of the kidneys, arteries, smooth muscles, lungs and other soft tissues. The provitamin D, previtamin D, **vitamin D**, active **vitamin D** and vitamin K of the ophthalmic or dermatological compositions of this invention have always been effective in smaller doses, and though some of the **vitamin D** or vitamin K may be absorbed into the blood through the eyes or skin, the side-effects seen with conventional preparations. . . .

AN 2000:171025 USPATFULL
PI US 6162801 20001219
WO 9718817 19970529

L3 ANSWER 16 OF 389 USPATFULL

SUMM . . . absorption curve for harmful UV radiation in the neighborhood of 260 nm, one or more of provitamin D, previtamin D, **vitamin D**, active **vitamin D**, vitamin K or an analog of any of these is used as the effective ingredient in the ophthalmic composition or dermatological composition. Effective forms of **vitamin D** include ergocalciferol or **cholecalciferol** as well as active forms of **vitamin D** formed by hydroxylation of the C1 position of the A-ring of the sterol nucleus, side-chain C25 or both C1 and C25. Considering that active **vitamin D** medicines have been used to treat psoriasis in the past, it is anticipated that the dermatological composition of this invention. . .

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WO 9718817 19970529

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(11) 特許出願公開番号

特開平8-245362

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|---------------------------|------|--------|--------------|--------|
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| | | | | W |
| 31/07 | ADA | | 31/07 | ADA |

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(22) 出願日 平成7年(1995)3月8日

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東京都文京区本駒込2丁目27番18-701号

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東京都小平市小川西町5丁目3番15号

(74) 代理人 弁理士 志村 光春

(54) 【発明の名称】 紫外線損傷防御外用剤

(57) 【要約】

【目的】紫外線の皮膚到達量を減少させる効果によるのみならず、紫外線による皮膚損傷予防活性及び損傷皮膚回復活性に基づき、皮膚障害の防御効果が飛躍的に向上した紫外線損傷防御外用剤の提供。

【構成】紫外線防御剤並びに正常皮膚機能維持活性成分及び損傷皮膚回復活性成分としてビタミンA、ビタミンAエステル及びビタミンA酸エステルからなる群より選ばれる1種又は2種以上のビタミンA類を含んでなることを特徴とする紫外線損傷防御外用剤。特に、上記ビタミンA類の配合比が、外用剤全体に対して、0.05重量%以上、2.0重量%以下である上記の紫外線損傷防御外用剤。

useful as **sunscreening** agents. None of the steroids described in these references however is a .DELTA..^{5,7} steroidal diene or .DELTA..^{3,5,7} steroidal triene.

SUMM Leigh, U.S. Pat. No. 3,981,996 describes **sunscreening** preparations comprising mixtures of vitamins A and D. It should be noted, of course, that **vitamin D** can be produced from provitamin D (a .DELTA..^{5,7} steroidal diene) by a sequence of photochemical and thermal isomerization steps.

SUMM . . . suggested the topical application of 1.alpha.,25-dihydroxy-7-dehydrocholesterol as being useful to deliver eq

L3 ANSWER 12 OF 389 CAPLUS COPYRIGHT 2001 ACS
 AB Topical preps. for preventing or reducing the damaging effects of
 UV-light on skin comprise 1-**hydroxycholecalciferol** and/or 1,25-
dihydroxycholecalciferol in combination with a **sunscreen**
 material and preferably also retinol and/or a deriv. thereof. A lotion
 contained 1,25-**dihydroxycholecalciferol** 0.5, retinol 2, volatile
 siloxane (DC 345 fluid) 8.2, silicone surfactant (DC 3225C) 12, mineral
 oil 1.5, petroleum jelly 0.5, . . .
 ST **cholecalciferol sunscreen** cosmetic
 IT **Sunscreens**
 Tocopherols
 RL: BIOL (Biological study)
 (cosmetics contg. **cholecalciferol** deriv. and, for skin
 protection from UV-light)
 AN 1993:27283 CAPLUS
 DN 118:27283
 PATENT NO. KIND DATE APPLICATION NO. DATE

 PI EP 512814 A1 19921111 EP 1992-304076 19920506
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, PT, SE

L3 ANSWER 3 OF 389 CAPLUS COPYRIGHT 2001 ACS
 TI .**Sunscreens** containing **vitamin D** derivatives
 and UV absorbers
 AB **Sunscreens**, which protect the skin from UV ray and keep good
 skin conditions, contain **vitamin D** derivs. and UV
 absorbers. Stearic acid 6.0, sorbitan monostearate 2.0, polyoxyethylene
 sorbitan monostearate 1.5, 2-(2'-hydroxy-5'-methylphenyl)benztriazole 8.0,
 propylene glycol 10.0, vitamin D2 0.05, antiseptic agent, antioxidant,
 perfume, and H2O to 100% were mixed to give a **sunscreen** cream.
 ST **sunscreen vitamin D** UV absorber
 IT 50-14-6, Vitamin D2 67-97-0, **Vitamin D3** 1173-13-3,
Precholecalciferol 1406-16-2, **Vitamin D**
 51744-66-2, 5,6-trans-Ergocalciferol
 RL: BIOL (Biological study)
 (sunscreens contg. UV absorbers and)
 AN 1994:14674 CAPLUS
 DN 120:14674
 PATENT NO. KIND DATE APPLICATION NO. DATE

 PI JP 05246835 A2 19930924 JP 1992-81599 19920303

L3 ANSWER 18 OF 389 CAPLUS COPYRIGHT 2001 ACS
AB .The title prepns. contain vitamin A, its esters, and/or vitamin
A acid esters as skin function activators, repair
enhancers for damaged skin, and UV **sunscreens**. An aq. soln.
contg. retinyl acetate, 2,2'-dihydroxy-4-methoxy-benzophenone, stearic
acid monoglyceride, etc., was applied to volunteers to prevent UV-induced
skin damage.

AN 1997:303406 CAPLUS
Correction of: 1996:709890

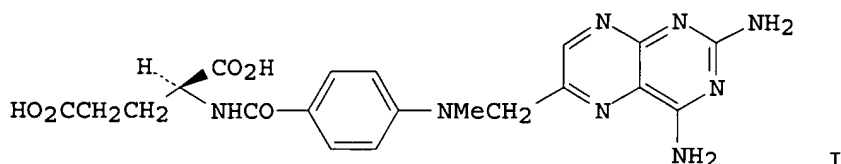
DN 126:282549
Correction of: 125:338745

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| PI JP 08245362 | A2 | 19960924 | JP 1995-77181 | 19950308 |

L13 . ANSWER 1 OF 7 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
 AN 1984-14515 DRUGU P B
 TI Percutaneous Penetration of Methylglyoxal Bis(guanylhyazone): Effects
 of Hairless Mouse Epidermis In Vivo.
 AU McCullough J L; Weinstein G D; Rosenblum M G; Jenkins J J
 LO Irvine, California, Houston, Texas, United States
 SO J.Invest.Dermatol. (81, No. 5, 388-92, 1983) 5 Fig. 3 Tab. 16 Ref.
 CODEN: JIDEAE ISSN: 0022-202X
 AV Department of Dermatology, University of California, Irvine, California
 College of Medicine, Irvine, California 92717, U.S.A.
 LA English
 DT Journal
 AB **Vehicle N** (VN, Neutrogena) **enhanced** the
 percutaneous **penetration** of mitoguazone (M, Aldrich) in human
 skin in vitro and in mouse skin. VN and n-decylmethyl sulfoxide (Cyclo
 Chem.) also increased epidermal content of M, compared to saline and
 N-methylpyrrolidone (Nelson) vehicles. Both topical and i.p. M increased
 S-adenosyl-L -methionine (SAM) decarboxylase. It is suggested that M in
 VN could be used in the treatment of psoriasis-type disorders.
 SH P Pharmacology
 B Biochemistry
 CC 8 Pharmacokinetics
 14 Enzyme Inhibitors
 22 Endogenous Compounds
 25 Neoplasia
 27 Molecular Biology
 29 Pharmaceutics
 36 Dermatological
 CT [01] MITOGUAZONE *DM; MITOGUAZONE *PH; ALDRICH *FT; TETRADECANOYLPHORBOL-
 ACETATE *RC; MOUSE *FT; HUMAN *FT; SKIN *FT; IN -VITRO *FT; IN-VIVO
 *FT; DERMATOLOGICAL *FT; TOPICAL *FT; I.P. *FT; CONC. *FT; EC-4.1.1.50
 *FT; NUCLEIC-ACID-METAB. *FT; DNA *FT; N -METAB. *FT; PUTRESCINE *FT;
 SPERMIDINE *FT; SPERMINE *FT; CONC. *FT; AUXILIARY-INGREDIENT *FT;
 NEUTROGENA *FT; BIOPHARM. *FT; PERCUTANEOUS *FT; ABSORPTION *FT;
 CYTOSTATICS *FT; LAB.ANIMAL *FT; ADENOSYLMETHIONINE-DECARBOXYLASE *FT;
 PHARMACEUTICS *FT; MITOGUAZO *RN; DM *FT; PH *FT
 FA AB; LA; CT; MPC
 FS Literature

=>

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2001 ACS
 AN 19820444209 CAPLUS
 DN .97:44209
 TI Percutaneous absorption of methotrexate: effect on epidermal DNA synthesis in hairless mice
 AU Ball, Marina A.; McCullough, Jerry L.; Weinstein, Gerald D.
 CS Dep. Dermatol., Univ. California, Irvine, CA, 92717, USA
 SO J. Invest. Dermatol. (1982), 79(1), 7-10
 CODEN: JIDEAE; ISSN: 0022-202X
 DT Journal
 LA English
 CC 63-5 (Pharmaceuticals)
 Section cross-reference(s): 1
 GI



AB Vehicles were investigated to optimize methotrexate (I) [59-05-2] penetration of skin in vitro, and the effects of a topical I formulation on epidermal DNA synthesis in vivo in the skin of hairless mice were studied. Skin penetration of I was greater with **Vehicle N** (laureth-4, 4% iso-PROH, propylene glycol, 47.5% EtOH, and H2O) than with H2O and n-decyl Me sulfoxide vehicles. Repeated application of I in **Vehicle N** produced marked epidermal atrophy in treated sites in both normal and hyperproliferative essential fatty acid deficient hairless mouse skin without similar effects at a distant skin site. Local inhibition of epidermal DNA synthesis was also obtained without systemic effects. Thus, I in **Vehicle N** may be useful for the topical therapy of psoriasis.
 ST methotrexate skin absorption vehicle; DNA epidermis inhibition methotrexate; psoriasis DNA methotrexate
 IT Deoxyribonucleic acid formation
 (by epidermis, of hairless mice, inhibition of, by methotrexate topical formulations)
 IT Deoxyribonucleic acids
 RL: FORM (Formation, nonpreparative)
 (formation of, in epidermis in hairless mice, inhibition of, by methotrexate topical formulations)
 IT Psoriasis
 (methotrexate absorption by skin in relation to treatment of)
 IT Skin, metabolism
 (epidermis, methotrexate absorption by, DNA formation inhibition in hairless mice in relation to)
 IT 59-05-2
 RL: BIOL (Biological study)
 (absorption of, by skin, epidermal DNA synthesis inhibition in relation to)

L3 ANSWER 2 OF 4 USPATFULL

SUMM. . . . exhibited small increases in penetration. Ball et al. (J. Invest. Dermatol. 79:710 (1982)) also observed an increase in penetration using "Vehicle N" (alcohol 47.5%, water, laureth 4, isopropyl alcohol 4%, propyleneglycol) from Neutrogena Corporation.

SUMM . . . patients. However, there were no statistical differences in drug treated versus vehicle treated sites one week after therapy was discontinued. **Enhancement** of methotrexate **penetration** into the affected skin in patients with psoriasis resulted in emprovement in the psoriatic plaques with no evidence of systemic. . . .

ACCESSION NUMBER: 92:92758 USPATFULL

TITLE: Methotrexate compositions and methods of treatment using same

INVENTOR(S): Loev, Bernard, Scarsdale, NY, United States

PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Fort Lee, NJ, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 5166149 | | 19921124 |
| APPLICATION INFO.: | US 1991-713558 | | 19910610 (7) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1989-404424, filed on 8 Sep 1989, now abandoned | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Waddell, Frederick E. | | |
| ASSISTANT EXAMINER: | Fay, Zohreh A. | | |
| LEGAL REPRESENTATIVE: | Kenyon & Kenyon | | |
| NUMBER OF CLAIMS: | 11 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 431 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.